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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,229	11/27/2001	Peter M. Bramley	B0192/7031	9395

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EXAMINER

KALLIS, RUSSELL

ART UNIT PAPER NUMBER

1638

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/890,229

Applicant(s)

BRAMLEY ET AL.

Examiner

Russell Kallis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 August 2004 and 06 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,7,10,11,14,15,24,25 and 28-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,7,10,11,14,15,24,25 and 28-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 August 2004 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 4/01/04
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of SEQ ID NO: 3 in the reply filed on 12/06/2004 is acknowledged. The traversal is on the ground(s) that the three sequences are linked by an inventive concept. This is not found persuasive because each polypeptide constitutes an independent and patentably distinct invention. Separate searches and considerations would be required for examination of each of the amino acid sequences.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-4, 7, 10-11, 14-15, 24-25 and 28-34 are pending and examined.

Rejection of claims 29, 33 and 34 under 35 U.S.C. 101 is withdrawn in view of Applicant's amendments.

Rejection of claims 24-25 and 29 under 35 U.S.C. 102(b) is withdrawn in view of Applicant's amendments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Drawings

The drawings are objected to because Figure 3 is largely illegible and lacks the drawing number i.e. 3/8. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the

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appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

Claim 29 is objected to because of the following informalities: Claim 29 recites "any of claims 24 to 28". The claim is dependent from canceled claims 26 and 27. Further, the dependency should be recited in the alternative "any one of Claims 24, 25 or 28". Appropriate correction is required.

Claim 25 is objected to for containing non-elected amino acid sequences.

Claim Rejections - 35 USC § 112

Claims 14-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. The added claimed material which is not supported by the original disclosure is as follows: Newly amended Claims 14-15 recite 'yeast', while the specification only supports plants cells, plants and bacteria. Moreover, the specification

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does not recite the term 'yeast' at all. Thus, the claims are drawn to NEW MATTER. Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-4, 7, 10-11, 14-15, 24 and 28-29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/18/2004. Applicant's arguments filed 8/20/2004 and 12/06/2004 have been considered but are not deemed persuasive.

Applicant asserts that they have described both a representative number of species and has described structural features common to the claimed genus of polypeptides having DXPS activity and that the cloning and characterization of polynucleotides encoding DXPS from a number of organisms is well known in the art (response pages 6-7). Applicant does not describe polynucleotides encoding a functional equivalent of a DXP synthases, or other DNA sequences that could be used to alter DXPS activity.

Claims 1-4, 7, 10-11, 14-15, 24-25 and 28-34 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of overexpression of DXPS in *E. coli* and increased lycopene and Co8 production, does not reasonably provide enablement for manipulating or increasing isoprenoid production in plants or other cells or organisms, other than *E. coli*, transformed with DXP synthase or any other combination of

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polynucleotides encoding an isoprenoid producing protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/18/2004. Applicant's arguments filed 8/20/2004 and 12/06/2004 have been considered but are not deemed persuasive.

Applicant asserts that Applicant was the first to show that expression of DXPS leads to increased IPP activity (response page 8 lines 8-9). Applicant has not measured IPP levels but only showed increased levels of lycopene, carotenoids and ubiquinone (UQ-8) in *E. coli* genetically transformed to produce lycopene further transformed with a DXPS gene that showed increased levels of lycopene relative to the transgenic control (specification, pages 22-24).

Applicant asserts that only routine experimentation would be required to practice the transformation of plants with DXPS and then test for increased isoprenoid levels (response page 9 line 17 to page 10 line 8). Applicant has not addressed the full enablement rejection that undue trial and error experimentation would be needed by one skilled in the art to make and clone a multitude of non-exemplified functional equivalents of DXP synthase or other DNA sequences that could be used to alter DXPS activity and would require one of skill in the art to test in a myriad of non-exemplified plants for increased DXP synthase and the level of some non-exemplified isoprenoid in a multitude of non-exemplified transformed plant species.

Applicant asserts that increasing the first step in the non-mevalonate pathway that is a rate limiting step will increase the overall level of isoprenoids and that the results of Shewmaker are not relevant to lack of enablement because Shewmaker manipulated a downstream step in isoprenoid biosynthesis (response page 10, lines 9-23). Although the art strongly suggests that

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DXPS governs a rate limiting step in isoprenoid biosynthesis the results of Shewmaker clearly indicate that DXPS is not the only rate limiting step in isoprenoid biosynthesis.

Claims 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites the limitation "said nucleic acid sequence encoding said DXPS" in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

Claims 1-4, 7, 10-11, 14-15, 24-25 and 29-31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Burkhardt P. *et al.*, The Plant Journal, 1997; Vol. 105, No. 5; pages 1071-1078; in view of Lange B. *et al.* PNAS March 3, 1998; Vol. 95, No. 5; pages 2100-2104. This rejection is maintained for the reasons of record set forth in the Official action mailed 2/18/2004. Applicant's arguments filed 8/20/2004 and 12/06/2004 have been considered but are not deemed persuasive.

Applicant broadly claims organisms; plant cells, plant tissue, plants, and yeast transformed with a DXP synthase a functional equivalent, or a nucleic acid that alters the activity of DXPS.

Burkhardt teaches transformation of rice by transformation via microprojectile bombardment using the full length daffodil *psy* gene operably linked to the CaMV 35S promoter; expression of the daffodil phytoene synthase in rice seeds including the amyloplast transit peptide under control of the endosperm specific rice glutelin promoter (Gt1) and the

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accumulation of nutritionally beneficial phytoene in rice endosperm (see Abstract and see page 1072, column 2, production of transgenic plants).

Burkhardt does not teach overexpression a DXP synthase gene in a plant.

Lange teaches overexpression in *E. coli* of a DXP synthase gene from *E. coli* wherein a start codon i.e. methionine is inherently taught, increased DXP synthase activity in transformed *E. coli* cells (see page 2103, column 2; in Results and Discussion); and the dxp synthase sequence of SEQ ID NO: 3 from *E. coli* on page 2102.

It would have been obvious at the time of Applicant's invention to modify the invention of Burkhardt to include overexpression of a DXP synthase gene encoding nucleic acid sequence from *E. coli*. One of skill in the art would have been motivated by the teachings of Lange that the mevalonate-independent pathway presents a unique opportunity for isoprenoid expression in bacteria and plants (see page 2104, column 1) and the success of Burkhardt in enhancing the expression of isoprenoids in rice by transformation with a nucleic acid encoding an isoprenoid producing enzyme i.e. phytoene synthase, and that one would have had a reasonable expectation of success of expressing genes in transformed plants and in plant and bacterial cells, wherein the choice of an endogenous or exogenous gene for genetically engineering an organism for increased isoprenoid expression is an obvious optimization of design parameters.

Applicant asserts that Burkhardt does not disclose that the first reaction in the mevalonate independent pathway is a rate limiting step and that enzymes involved in the isoprenoid pathway other than phytoene synthase can be overexpressed (response page 13 lines 10-14). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the first reaction in the

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mevalonate independent pathway is a rate limiting step and that enzymes involved in the isoprenoid pathway other than phytoene synthase can be overexpressed) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, Burkhardt does teach accumulation of phytoene in the endosperm of rice transformed with phytoene synthase thus providing both motivation to further pursue genetic engineering increases in isoprenoid biosynthesis in plants and providing a reasonable expectation of success.

Applicant asserts Lange does not teach that the first reaction in the mevalonate independent pathway is a rate limiting step and there is no indication in Lange that the conversion catalyzed by DXPS is in fact of great importance in the IPP biosynthetic pathway (response page 13 lines 9-24). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the first reaction in the mevalonate independent pathway is a rate limiting step and there is no indication in Lange that the conversion catalyzed by DXPS is in fact of great importance in the IPP biosynthetic pathway) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, Lange teaches that the on-mevalonate pathway is present in plants and operates in parallel with the cytosolic mevalonate pathway to IPP to produce a broad array of isoprenoid compounds (Lange; see page 2104 column 1 lines 13-17). In addition, IPP is not an isoprenoid.

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Applicant further asserts that Lange provides no motivation to modify the teachings of Burkhardt because the isoprenoid pathway in plants is complex that it is not reasonable to conclude that because one enzyme when over expressed resulted in increased isoprenoids any enzyme when overexpressed would lead to an increase in isoprenoid biosynthesis; and further asserts that without Applicant's teachings one would not have a reasonable expectation of success (response pages 14-15); Lange provides motivation and a reasonable expectation of success in manipulating isoprenoid biosynthesis via IPP synthesis (see page 2104 column 1 lines 7-29). Moreover, Applicant has not presented any unexpected results as to the increased production of isoprenoids or IPP in plant cells, plant tissue, plants or yeast transformed with a DXPS polynucleotide, a functional equivalent or a nucleic acid that alters DXPS activity.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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No claim is allowed.

Claims 28 and 32-34 are declared free of the prior art given the failure of the prior art to teach or reasonably suggest a transgenic tomato plant transformed a nucleic acid encoding a DXP synthase.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Russell Kallis Ph.D.
March 2, 2005

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized flourish at the end.

**AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**